

Cystic Fibrosis of the Pancreas

Diagnosis by Sodium Electrode Sweat Tests

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■ *One of the most difficult and unreproducible procedures in clinical laboratories has been the measurement of electrolytes in sweat. The iontophoresis techniques for the diagnosis of cystic fibrosis of the pancreas, which are widely used, are fraught with difficulties.*

Measurement of sweat electrolytes with sodium or chloride electrodes is gradually replacing the iontophoresis methods. A simple modification of the sodium electrode technique was used for diagnosis in 11 cystic fibrosis patients and in 260 normal children. The values obtained with the sodium electrode clearly separated the normal children from those with cystic fibrosis.

IN RECENT YEARS, iontophoresis has been used extensively to measure sweat electrolytes to diagnose cystic fibrosis of the pancreas.¹ The iontophoresis technique has been a very difficult procedure in most laboratories, and carries a slight risk to the patient. In infants it is often impossible to obtain enough sweat by iontophoresis to give accurate electrolyte measurements. An important contribution to the diagnosis of cystic fibrosis was made by Goldbloom and Sekelj,² who developed an ingenious technique for determining the sodium concentration of sweat, using a special sodium electrode applied to the skin surface. Warwick³ described a modified heated chloride electrode test, which is somewhat more complicated than the procedure we are using. The technique of Hansen and coworkers,⁴ using a chloride electrode, is more complicated and time-consuming.

Since June 1964, we have used the sodium electrode in place of iontophoresis to determine sweat sodium ion concentration. We have modified the technique of Goldbloom and Sekelj, using a simpler method. This report confirms the findings of Goldbloom and Sekelj and describes the use of the sodium electrode with our modified technique in 22 normal adults, 11 children with cystic fibrosis, and 260 normal children.

Instrumentation and Methods

A Beckman combination electrode A 78420V was used to measure the concentration of sodium ion on the surface of the skin. This electrode, unlike the usual glass electrode, is filled with a mixture of KCl and AgCl. A Beckman pH meter-voltmeter was used to measure direct voltage, employing the expanded scale. The electrode when first put into use was calibrated by measuring the potentials obtained with solutions of known sodium ion concentration at various temperatures. The values were plotted on semi-log paper. Slight

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differences in the potentials were found at different temperatures. Goldbloom and Sekelj used a thermistor to correct for variations in the skin temperatures of the patients.

To eliminate the use of a thermistor, we developed a technique in which the voltage obtained from the center of the patient's palm was compared with the voltages obtained after thin layers of at least three standard solutions of sodium ions, poured onto the palm, were allowed to equilibrate with the skin temperature. Equilibration occurred within a few seconds. This technique corrected for skin temperature and also gave a new accurate calibration curve for each case. To determine the patient's own sweat sodium concentration, the patient's hands were washed with soap, thoroughly rinsed with tap water, rinsed with distilled water, and dried with clean towels or Kimwipes® (absorbent paper). Kimwipes or properly laundered towels did not change the sweat sodium. The rubber collar was slipped above the round opening in the electrode glass before use. The electrode was then applied against the skin with an even firm pressure. For the measurement of the intrinsic sweat sodium concentration, it was necessary to wait about three minutes after drying the skin, to allow enough sweat to appear on the skin surface to give accurate, stable voltage readings. We did not find it necessary to use external heat in the manner described by Hansen and coworkers.⁴ The waiting period was not necessary in measuring the potentials of the standard solutions on the skin. The tests were done in duplicate or triplicate.

Between applications of the electrode to the skin, the tip of the electrode was washed with distilled water from a squeeze bottle and gently wiped with Kimwipes. We found that the sodium concentration of the sweat of the skin in the center of the palm was different from the concentration in the skin overlying the metacarpal folds and the thenar and hypothenar eminences. The center of the palm was the most convenient area for determining voltages.

If the electrode was stored in distilled water or in a high concentration of sodium ion, its performance was erratic, with considerable instability and voltage drifting. This instability was avoided by immersing the electrode in a standard 10 mEq per liter sodium solution when not in use. Sodium standards were easily prepared from our stock solutions used for flame photometry. Working solutions of standard containing 10, 25, 50, 75,

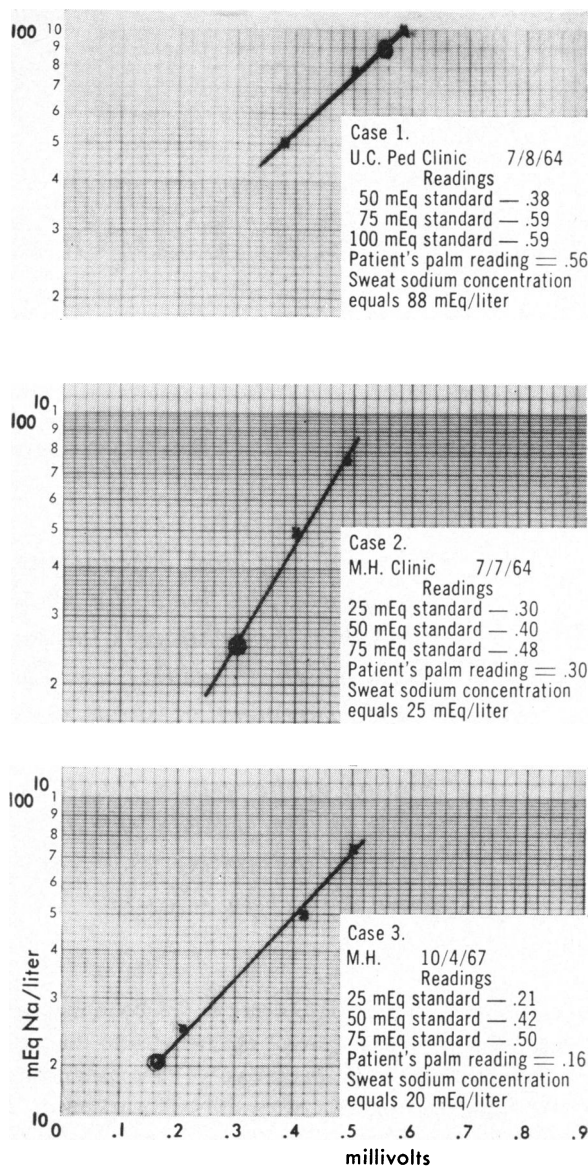


Chart 1.—Sweat sodium concentration measurements on one patient with cystic fibrosis (Case 1) and two normal children (Cases 2 and 3).

100 and 125 mEq of sodium per liter were used. Higher concentrations were required in a few cases. The standards employed in each test were selected to give potentials bracketing the intrinsic potential found on the skin. The voltage readings of the standards were plotted on three-cycle semi-logarithmic paper (Chart 1), usually used for three tests, and the voltage reading of the patient's palm was converted to mEq Na per liter from the straight line obtained with the standards (Chart 1). Unlike the usual glass electrodes used for pH

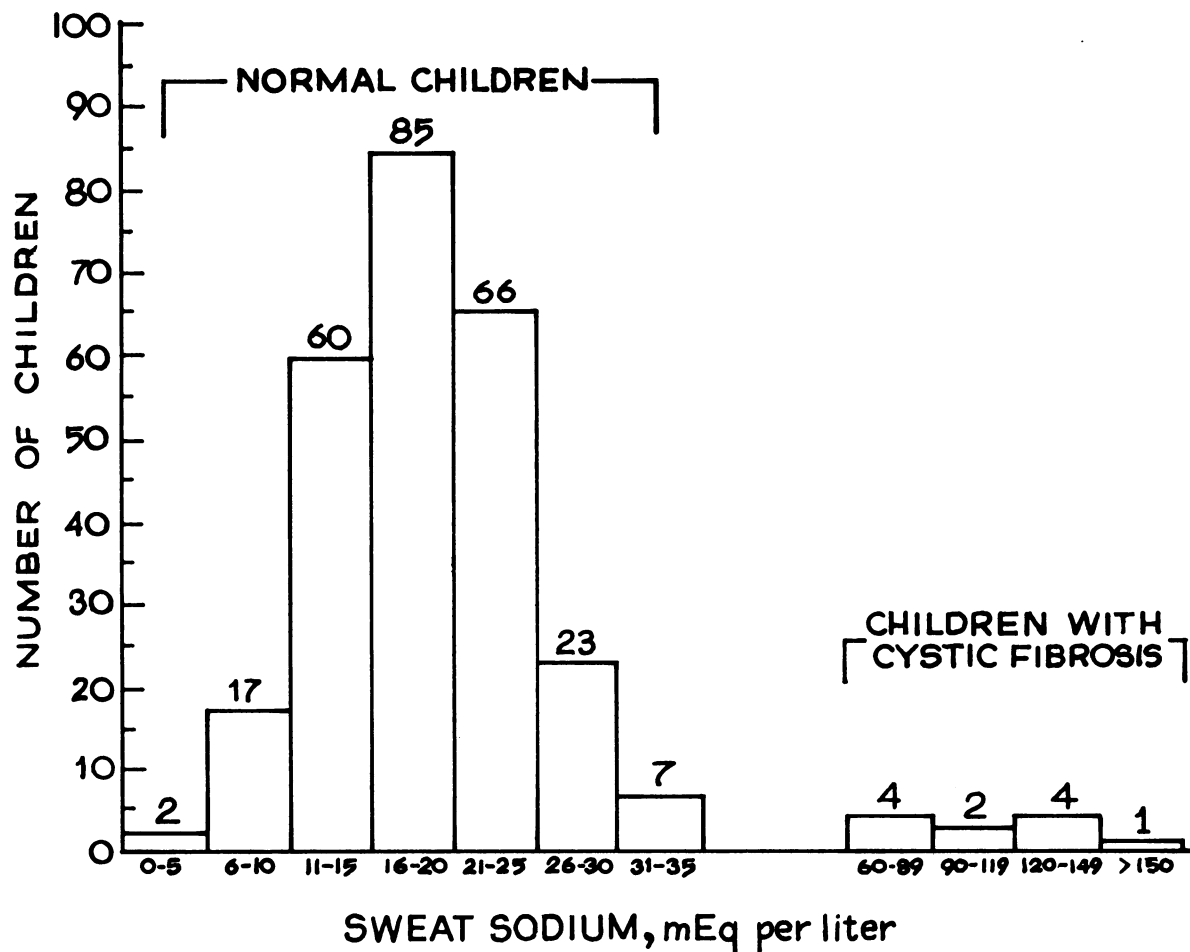


Chart 2.—Note that the highest sweat sodium value in 260 normal children was 35 mEq per liter. In the 11 cystic fibrosis patients, the sweat sodium varied from 60 to 184 mEq per liter.

determinations, the sodium electrode was not rendered unstable by static electricity. On two occasions, technicians when storing the electrode in 10 mEq NaCl left the rubber collar off the round hole in the electrode glass wall, and the NaCl solution mixed by convection with the KCl-AgCl solution within the electrode, so that readings were unobtainable. This defect was easily corrected by emptying the electrode with Pasteur pipettes, and refilling with the proper KCl-AgCl solution.

Patient Material

Electrode sweat sodium concentrations first were measured in normal adults in our laboratory. In June, 1964, through the courtesy of Dr. Louise Yeazell, Associate Professor of Pediatrics at the University of California, and with the help of Dr. Herman Lipow, who was working in the Cystic

Fibrosis Clinic at that time, our instruments and solutions were taken by one of us (S.F.) on several occasions to the University of California Cystic Fibrosis Clinic, and measurements were taken on six children with known cystic fibrosis, and on ten patients who were considered normal. In our laboratory we have studied over 255 children from Mercy Childrens Hospital and Mercy Hospital Childrens Clinic, as well as patients referred from other hospitals. Five of these patients had high sweat sodium levels correlated with cystic fibrosis.

Results

Chart 1 compares the findings in two normal persons and one cystic fibrosis patient, and demonstrates our method of calculating results on semi-log paper. Chart 2 is a frequency distribution curve

showing the sweat sodium concentrations of 260 normal children and 11 children with known cystic fibrosis. None of the normal adults had sweat sodium concentrations higher than 50 mEq per liter. None of the normal children had sweat sodium concentrations higher than 35 mEq per liter, and the mean was 19 mEq. The lowest sweat sodium concentration in a patient with cystic fibrosis was 60 mEq per liter. The mother of two brothers with cystic fibrosis had a sweat sodium concentration of 67 mEq per liter. The father of this patient had a sweat sodium concentration of 41 mEq per liter.

Discussion

In our experience, the sodium electrode is the best instrument for the determination of sweat sodium ion concentrations. With the iontophoresis technique it is often impossible to get enough sweat from babies to give accurate results. The iontophoresis procedure took at least two hours of a technician's time, compared with 15 or 20 minutes required to obtain duplicate standardizing curves and sweat tests with the sodium electrode.

The application of standard solutions to the patient's skin corrects for the temperature variations in the skin. In all of our curves, at least three points were determined with different sodium standards on the skin, and these points almost always produced a straight line on semi-log paper. If a straight line was not produced, either one of

the standards was inaccurate or the reference battery of the pH meter-voltmeter needed to be replaced. The reference battery should be replaced every four months. The electrodes lasted about 18 months.

The findings with the sodium electrode were comparable to those obtained with a chloridometric method used at the University of California. We have not presented the correlation with those chloridometric determinations, because those measurements were made one to six weeks before our tests. The values we obtained with our previous iontophoresis-flame photometer sodium and colorimetric chloride tests were not reproducible enough to be used to check the sodium electrode method, which was reproducible.

A high sweat sodium concentration test alone does not make the diagnosis of cystic fibrosis. However, in all of our patients there was a sharp differentiation between normal and abnormal findings, which correlated well with the clinical diagnosis.

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MALABSORPTION OF FAT DUE TO CHOLESTYRAMINE

"One of a number of drugs that can significantly alter the intraluminal environment of the gut is the anion exchange resin cholestyramine (Cuemid or Questran) used for relief of itching in jaundiced patients and suggested for use in lowering serum cholesterol. This agent binds bile salts within the intestinal lumen. The amount of bile salts then available for micelle formation, which is necessary for normal fat absorption to proceed, is thus greatly reduced; and significant malabsorption of fat results whenever cholestyramine is administered in large doses."

—JERRY S. TRIER, M.D., Albuquerque

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